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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/830,968	11/06/2001	Carlos Miguel Carcagno	1909.0040002	7301
7590 09/21/2006 Sterne Kessler Goldstein & Fox Suite 600 1100 New York Avenue NW Washington, DC 20005-3934			EXAMINER KAUSHAL, SUMESH	
			ART UNIT 1633	PAPER NUMBER

DATE MAILED: 09/21/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/830,968

Applicant(s)

CARCAGNO ET AL.

Examiner

Sumesh Kaushal Ph.D.

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 06 July 2006.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-5, 7-13 and 15-20 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-5, 7-13 and 15-20 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date _____
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date _____
- 5) ☐ Notice of Informal Patent Application
- 6) ☐ Other: _____

DETAILED ACTION

Applicant's response filed on 07/06/06 has been acknowledged.

Claims 1-5, 6-13 and 15-20 are pending and are examined in this office action.

Applicants are required to follow Amendment Practice under revised 37 CFR §1.121. The fax phone numbers for the organization where this application or proceeding is assigned is 571-273-8300.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The references cited herein are of record in a prior Office action.

Response to Arguments

Applicant's arguments filed 07/06/06 and 10/13/05, with respect to the prior art rejection(s) under 35 USC 103 have been fully considered and are persuasive. Therefore, the rejection has been withdrawn. However, upon further consideration, a new ground(s) of rejection is made as stated below.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-5, 7-13 and 15-20 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement (new matter). The claim(s)

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contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The applicant amended the instant claims in the response filed on 04/21/05 to limit the scope of claim 1 to "culture medium consisting of DMEM (Dulbecco's modified Eagle's medium), F12 medium, insulin and one or more additives selected from the group consisting of NaHCO₃, sugars, ethanolamine, pyruvate, amino acids and mixtures thereof". The applicant states that support for such amendment could be found on page 14 of the instant specification. However, page 14 of the instant application fails to disclose a culture media that consist of consisting of DMEM (Dulbecco's modified Eagle's medium), F12 medium, insulin and one or more additives selected from the group consisting of NaHCO₃, sugars, ethanolamine, pyruvate, amino acids and mixtures thereof". The scope of culture media as claimed herein is broader than the culture media disclose on page 14 (see culture media no.3).

As MPEP 2163.06 notes " If new matter is added to the claims, the examiner should reject the claims under 35 U.S.C. 112, first paragraph - written description requirement. In re Rasmussen, 650 F.2d 1212, 211 USPQ 323 (CCPA 1981)." So claims 1-5, 6-13 and 15-20 are apparently new matter. A careful review by the examiner of the specification failed to identify any support for this new limitation. Since no basis has been found to support the new claim limitation in the specification, the claims are rejected as incorporating new matter.

Claims 1-5, 7-13 and 15-20 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Nature Of Invention

The instant invention relates to large scale production of recombinant production of rEPO in mammalian cells

Breadth Of Claims And Guidance Provided in the Specification

The scope of invention as claimed encompasses a method for obtaining human erythropoietin comprising culturing mammalian cells which express recombinant human erythropoietin in culture medium consisting of DMEM, F12 medium, insulin and one or more additives selected from the group consisting of NaHCO₃, sugars, ethanolamine, pyruvate, amino acids and mixtures thereof. At best the specification teaches maintaining growth and proliferation of recombinant CHO(rEPO) cells using a culture media containing Fetal calf serum followed by harvesting of rEPO in a serum free media. The specification fails to disclose growth and proliferation of recombinant CHO, COS, BHK, Namalwa and HeLa cells for the production of rEPO in serum free culture media (as claimed).

State Of Art And Predictability

The state of art at the time of filing teaches various factors affect the production of recombinant proteins in serum free medium. Several culture parameters could affect the metabolism of cultured cells and hence affect the glycosylation and sialylation of secreted glycoproteins. These factors include combination of nutrition, concentration and accumulation of by products. (see Wang et al Biotechnol Bioeng. 77(2):194-203. 2002, Yang et al, Biotechnol Prog. 18(1):129-38., 2002 Schroder et al J Biotechnol. 108(3):279-92, 2004). Therefore the combination of essential nutrients (sugars, salts and growth factors etc) and their concentration varies not only with choice of host cells but also depends upon the selection of culture conditions. For example, recombinant production of EPO could be best achieved by using a basal medium prepared by supplementing Iscove's modified Dulbecco's medium (IMDM) with Fe(NO₃)₃·9H₂O, CuCl₂ and ZnSO₄·7H₂O along with Insulin, transferrin and ethanolamine in optimal concentrations (see Lee et al J Biotech. 69:85-93, 1999. ref of record). In the instant case, besides the set of sequential culture conditions that sustains the growth and proliferation of CHO cells (in order to produce rEPO), the specification as filed fails to

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disclose any other culture conditions (i.e. composition of nutrients used) for COS, BHK, Namalwa and HeLa cells especially context with the production of rEPO in serum free culture media as claimed. The state of the art clearly teaches that adaptation of cell lines to serum free conditions is critical step in order to sustain viability and growth of recombinant cells, which not only requires stepwise weaning of serum conditions but also the addition of various additives to the culture media in order to produce a particular recombinant protein of interest. The USPTO does not have laboratory facilities to test if an invention will function as claimed when working examples are not disclosed in the specification, therefore, enablement issues are raised and discussed based on the state of knowledge pertinent to an art at the time of the invention, therefore skepticism raised in the enablement rejections are those raised in the art by artisans of skill. Furthermore, It is noted that patent protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable (See *Brenner v. Manson*, 383 U.S. 519, 536, 148 USPQ 689, 696 (1966), *Stating, in context of the utility requirement, that "a patent is not a hunting license. It is not a reward for the search, but compensation for its successful conclusion."*) Tossing out the mere germ of an idea does not constitute enabling disclosure. While every aspect of a generic claim certainly need not have been carried out by an inventor, or exemplified in the specification, reasonable detail must be provided in order to enable members of the public to understand and carry out the invention. At issue, under the enablement requirement of 35 U.S.C. 1 12, first paragraph is whether, given the Wands-factors, the experimentation was undue or unreasonable under the circumstances. "Experimentation must not require ingenuity beyond that to be expected of one of ordinary skill in the art." See *Fields v. Conover*, 443 F.2d 1386, 170 USPQ 276 (CCPA 1970). *In instant case large scale industrial production of rEPO in serum free conditions (as claimed) is not considered routine in the art and without sufficient guidance to the contents and their concentrations in the culture media used the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue.* See *In re Wands* 858 F.2d 731, 8 USPQ2d 1400 (Fed. Cir, 1988). It is noted that the unpredictability of a particular area may alone provide

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reasonable doubt as to the accuracy of the broad statement made in support of enablement of claims. See *Ex parte Singh*, 17 USPQ2d 1714 (BPAI 1991). Therefore considering the state of the art and limited amount of guidance provided in the instant specification, one skill in the art would have to engage in excessive and undue amount of experimentation to exercise the invention as claimed.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-5, 7-13 and 15-20 rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

A broad range or limitation together with a narrow range or limitation that falls within the broad range or limitation (in the same claim) is considered indefinite, since the resulting claim does not clearly set forth the metes and bounds of the patent protection desired. See MPEP § 2173.05(c). Note the explanation given by the Board of Patent Appeals and Interferences in *Ex parte Wu*, 10 USPQ2d 2031, 2033 (Bd. Pat. App. & Inter. 1989), as to where broad language is followed by "such as" and then narrow language. The Board stated that this can render a claim indefinite by raising a question or doubt as to whether the feature introduced by such language is (a) merely exemplary of the remainder of the claim, and therefore not required, or (b) a required feature of the claims. Note also, for example, the decisions of *Ex parte Steigewald*, 131 USPQ 74 (Bd. App. 1961); *Ex parte Hall*, 83 USPQ 38 (Bd. App. 1948); and *Ex parte Hasche*, 86 USPQ 481 (Bd. App. 1949). In the present instance, claim 1 recites the broad recitation "*one or more additives selected from the group consisting of NaHCO₃, sugars, ethanalamine, pyruvate, amino acids and mixtures thereof*", and the claim also recites culture media "consisting of" which is the narrower statement of the range/limitation.

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Claim 1 is rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The omitted steps are: isolation of human erythropoietin from said mammalian cell culture.

Double Patenting

Claims 1-5, 6-13 and 15-20 stand rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1 and 7-13 of U.S. Patent No. 6,777,205, for the same reasons of record as set forth in the office action mailed on 12/29/05.

Applicant is considering submitting a terminal disclaimer in accordance with 37 C.F.R. § 1.321(c) upon the notification by the Examiner of allowable subject matter.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sumesh Kaushal Ph.D. whose telephone number is 571-272-0769. The examiner can normally be reached on Mon-Fri. from 9AM-5PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dave Nguyen can be reached on 571-272-0731.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to **571-272-0547**. For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199. The fax phone number for the organization where this application or proceeding is assigned is **571-273-8300**



SUMESH KAUSHAL, PH.D.
PRIMARY EXAMINER